

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Currently Amended) A method of decreasing intraocular pressure or improving ocular accommodation in an animal, including a human, comprising administering an intraocular pressure decreasing or accommodation improving amount of (A) a compound of formula (I):



wherein:

- a. Ar is a ~~five or~~ six membered heteroaryl ring having a first ring nitrogen and optionally second or third ring nitrogens, with the remaining ring atoms being carbon, oxygen, or sulfur, ~~provided the first nitrogen of Ar is a quaternary nitrogen and Ar is not thiazolium, oxazolium or imidazolium;~~
- b. Y is substituted on the first ring nitrogen, ~~with the proviso that if Ar is pyrazole, indazole, (1,2,3) triazole, benzotriazole, or (1,2,4) triazole, the second ring nitrogen is substituted with~~
 1. ~~alkyl or alkoxycarbonylalkylene;~~
 2. ~~Ar*, {wherein, consistent with the rules of aromaticity, Ar* is C₆- or C₁₀-aryl or a 5- or 6-membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3) triazine, (wherein the ring fusion is at a carbon-carbon double bond of Ar*)}; or~~
 3. ~~Ar*alkyl, Ar*C(O)alkyl, Ar*sulfonylalkyl, or Ar*sulfinylalkyl; and~~
- c. Ar can be substituted on the ring carbon atoms
 1. with one or more substituents independently selected from the group consisting ω -alkylenesulfonic acid, carbamoyl, Ar*, Ar*-alkyl-, Ar*-O-, Ar*SO₂-, Ar*SO-, Ar*S-, Ar*SO₂NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-; or
 2. two adjacent substitutions together with their ring carbons form a C₆- or C₁₀-aromatic fused ring system; or
 3. two adjacent substitutions together with their ring carbons form a C₅-C₇ fused cycloalkyl ring having up to two double bonds including the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. two adjacent substitutions together with their ring carbons form a fused five to eight membered heterocycle, wherein the ring fusion is at the carbon-carbon double bond of Ar, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and S(O)_n, wherein n=0,1, or 2; or
5. two adjacent substitutions together with their ring carbons form a fused five or six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur;

d. Y is:

1. a group of the formula $-\text{CH}(\text{R}^5)-\text{R}^6$

- (a) R^5 is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, hydroxyalkyl, aminoalkyl-, dialkylaminoalkyl-, (N-[C₆ or C₁₀]aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, pyrrolidin-1-ylalkyl, azetidinyalkyl, 4-alkylpiperazine-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4-[C₆ or C₁₀]aryl piperazin-1-ylalkyl, 4-[C₆ or C₁₀]aryl piperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperazin-1-ylalkyl, piperidin-1-ylalkyl, [C₆ or C₁₀]aryl, or independently the same as R^6 ;
- (b) wherein R^6 is
 - (1) hydrogen, alkyl, (which may be substituted by alkoxy carbonyl)-, alkenyl, alkynyl, cyano-, cyanoalkyl-, or R_s , wherein R_s is a [C₆ or C₁₀]aryl or a heteroaryl containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen, and sulfur; or
 - (2) a group of the formula $-\text{W}-\text{R}^7$, wherein R^7 is alkyl, alkoxy, hydroxy, or R_s wherein W is $-\text{C}(=\text{O})-$ or $-\text{S}(\text{O})_2-$;
 - (3) a group of the formula $-\text{W}-\text{OR}^8$ wherein R^8 is hydrogen or alkyl,
 - (4) a group of the formula $-\text{CH}(\text{OH})\text{R}_s$; or
 - (5) a group of the formula $-\text{W}-\text{N}(\text{R}^9)\text{R}^{10}$, wherein
 - (a) R^9 is hydrogen and R^{10} is an alkyl or cycloalkyl, optionally substituted by
 - (i) [C₆ or C₁₀]aryl, or
 - (ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains at least one and up to three atoms of N and, the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl

ring can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C₆ or C₁₀]aryl piperazin-1-yl, 4-[C₆ or C₁₀]aryl piperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C₁-C₃)alkylenedioxy groups, or fused to a phenyl or pyridine ring, wherein the ring fusion is at a carbon-carbon double bond of the heteroaryl ring), or

(iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

(b) R⁹ is hydrogen or alkyl and R¹⁰ is Ar*^{*}; or

(c) R⁹ is hydrogen or alkyl, R¹⁰ is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur; or

(d) R⁹ and R¹⁰ are both alkyl groups; or

(e) R⁹ and R¹⁰ together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C₆-or C₁₀)aryl, (C₆-or C₁₀)arylalkyl, or a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings, each such heteroaryl can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C₆ or C₁₀]aryl piperazin-1-yl, 4-[C₆ or C₁₀]aryl piperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C₁-C₃)alkylenedioxy; or

(f) R⁹ and R¹⁰ are both hydrogen; or

2. -NH₂, and

(e)-X is a pharmaceutically acceptable anion, which may be absent if the compound provides a neutralizing salt, or

~~(B)~~-a pharmaceutically acceptable salt of the compound,

wherein aryl, Ar or Ar* can be substituted with, in addition to any substitutions specifically noted, with one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl,

alkoxycarbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar^{*}C(O)-, Ar^{*}C(O)NH-, Ar^{*}O-, Ar^{*}-, Ar^{*}-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid (SO₃H), 1-pyrrolidinyl-, 4-[C₆ or C₁₀]arylpiperazin-1-yl, 4-[C₆ or C₁₀]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

wherein heterocycles, except those of Ar or Ar^{*}, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar^{*}(CO)-, Ar^{*}O-, Ar^{*}-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

Claim 2. (Original) The method of claim 1, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula -CH(R⁵)R⁶.

Claim 3. (Original) The method of claim 2, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula -CH(R⁵)-W-R⁷.

Claim 4. (Original) The method of claim 2, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula -CH(R⁵)-W-Rs.

Claim 5. (Currently Amended) The method of claim 1, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein:

a e. Ar can be substituted on ring carbon atoms

1. with one or more substituents independently selected from the group consisting of hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy, (C₂-C₆)hydroxylalkyl, mercapto, nitro, sulfamoyl, sulfonic acid (-SO₃H), alkylsulfonyl (alkylSO₂-), alkylsulfinyl (alkylSO-) alkylthio,

trifluoromethyl, Ar*, Ar*-alkyl-, Ar*-O-, Ar*SO₂-, Ar*SO-, Ar*S-, Ar*SO₂NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-, wherein Ar* may be substituted by one or more substituents as set forth above; or

2. two adjacent substituents together with their ring carbons form a C₆- or C₁₀- aromatic fused ring system; or
3. two adjacent substitutions together with their ring carbons form a fused C₅-C₇ fused cycloalkyl ring having no double bonds except the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, amino, aminocarbonyl, carboxy, fluoro, or oxo, wherein multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl, and fluoro substituents, which can be located on the same or different carbon atoms;

b d. Y is:

1. a group of the formula -CH(R⁵)-R⁶
 - (a) R⁵ is hydrogen or alkyl;
 - (b) wherein R⁶ is
 - (1) hydrogen, alkyl, alkenyl, alkynyl, cyano, cyanoalkyl, or Rs, wherein Rs is a [C₆ or C₁₀]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or
 - (2) a group of the formula -W-R⁷, wherein R⁷ is alkyl, alkoxy, hydroxy, or Rs, wherein W is -C(=O)- or -S(O)₂-;
 - (3) a group of the formula -W-OR⁸ wherein R⁸ is hydrogen or alkyl,
 - (4) a group of the formula -CH(OH)Rs; or
 - (5) a group of the formula -W-N(R⁹)(R¹⁰), wherein
 - (a) R⁹ is hydrogen and R¹⁰ is an alkyl or cycloalkyl, optionally substituted by
 - (i) [C₆ or C₁₀]aryl, or
 - (ii) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl ring and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl ring; said heteroaryl ring can be optionally substituted with one or more halo or (C₁-C₃)alkenyldioxy groups, or fused to a phenyl ring, or

- (b) R^9 is hydrogen or alkyl and R^{10} is Ar^* ; or
~~(e)-(c)~~ R^9 and R^{10} together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with $(C_6\text{-or } C_{10})$ aryl, $(C_6\text{-or } C_{10})$ arylalkyl, or a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings, each such heteroaryl can be optionally substituted with one or more halo or $(C_1\text{-}C_3)$ alkylenedioxy; or
~~(d)~~ R^9 and R^{10} are both hydrogen;

or

2. $-NH_2$, and

~~e-~~X is a pharmaceutically acceptable anion, which may be absent if the compound provides a neutralizing salt, or

~~(B)~~a pharmaceutically acceptable salt of the compound,

wherein aryl, Ar or Ar^* can be substituted with, in addition to any substitutions

specifically noted, with one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, $(C_1\text{-}C_3)$ alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω -alkylenesulfonic acid, alkylthio, allyl, $Ar^*C(O)-$, $Ar^*C(O)NH-$, Ar^*O- , Ar^*- , $Ar^*\text{-alkyl-}$, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, $(C_2\text{-}C_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid (SO_3H); and

wherein heterocycles, except those of Ar or Ar^* , can be substituted with, in addition to

any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, $Ar^*C(O)-$, Ar^*O- , Ar^*- , carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl, wherein multiple substituents are located on different atoms of the heterocyclic ring, with the proviso that alkyl, alkylcarbonyl, and fluoro substituents can be substituted on the same carbon atom of the heterocyclic ring.

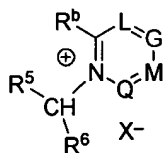
Claim 6. (Original) The method of claim 5, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula $-\text{CH}(\text{R}^5)-\text{W}-\text{R}^6$.

Claim 7. (Original) The method of claim 6, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula $-\text{CH}(\text{R}^5)-\text{W}-\text{R}^7$.

Claim 8. (Original) The method of claim 6, comprising administering an intraocular pressure decreasing or accommodation improving amount of a compound of formula I, wherein Y is according to formula $-\text{CH}(\text{R}^5)\text{-W-Rs}$.

Claims 9-15. (Cancelled)

Claim 16. (Currently Amended) The method of claim 1, wherein $Y-Ar\oplus \bullet X$ is



wherein L, G, M, Q, or R are independently N, C-R^c, C-R^d, C-R^e, C-R^f;

wherein

1. R⁵ is H;
2. R⁶ is
 - (1) cyano or
 - (2) a group of the formula -W-R⁷, wherein R⁷ is alkyl or Rs, and W is -C(=O)- or -S(=O)-;
3. R^b, R^c, R^d, and R^e are
 - (a) independently selected from the group consisting of hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar^{*}C(O)-, Ar^{*}O-, Ar^{*}-, Ar^{*}-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, sulfamoyl,

sulfonic acid (SO_3H), 1-pyrrolidinyl-, 4-[C_6 or C_{10}]aryl piperazin-1-yl, 4-[C_6 or C_{10}]aryl piperdin-1-yl, azetidin-1-yl, and morpholin-4-yl, piperidin-1-yl;

- (b) where any two of R^b , R^c , R^d , and R^e are adjacent, together with their ring carbons form a C_6 - or C_{10} - aromatic fused ring system;
- (c) where any two of R^b , R^c , R^d , and R^e are adjacent, together with their ring carbons form a C_5 - C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxy carbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo;
- (d) wherein any two of R^b , R^c , R^d , and R^e are adjacent, together with their ring carbons form a fused five to eight membered heterocycle, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and $\text{S}(\text{O})_n$ wherein $n=0,1$, or 2 ;
- (e) wherein any two of R^b , R^c , R^d , and R^e are adjacent, together with their ring carbons form a fused five or six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur, and wherein Ar has no more than three nitrogen atoms in the ring.

wherein Ar has no more than three nitrogen atoms in the ring.

Claim 17. (Original) The method of claim 1, wherein Ar is substituted on a said ring nitrogen with amino.

Claim 18. (Original) The method of claim 17, wherein Ar is further substituted with up to two aminos.